Defining Shock: Shock is a complex clinical syndrome caused by an acute failure of circulatory function, with inadequate tissue and organ perfusion, where delivery of oxygen and substrates to body tissues, as well as removal of metabolic waste products are insufficient. Sepsis is defined as abnormal temperature or leukocyte count, in addition to other abnormal vital signs, in the presence of proven or known invasive infection. Severe sepsis is defined as sepsis in combination with either cardiovascular organ dysfunction or acute respiratory distress. This condition may also exist when sepsis is combined with two or more other organ dysfunctions, including neurologic, renal, hepatic or hematologic systems. In children, septic shock is defined as proven or suspected infection with the presence of tachycardia and poor perfusion with or without hypotension.

Epidemiology: Nationally, there are over 75,000 hospitalizations for severe sepsis per year. The incidence is highest in newborns and falls dramatically in older children. The risk of death increases with increasing numbers of failing organs, from 7% for those with single-organ system failure to 53.1% for those with four organ systems or more failing. In 2013, an estimated 1860 patients were treated at Texas Children’s Hospital (TCH) in septic shock.

Etiology: The presumed most common causes of septic shock are of bacterial origin; however, any organism can precipitate septic shock, including bacteria, viruses, and fungi, especially in the immunocompromised patient. In 2012, the most common pathogens identified in a cohort of previously healthy patients at Texas Children’s Hospital (TCH) in septic shock were *Staphylococcus aureus*, *Streptococcus pneumoniae* and *group B streptococcus*. During the same time period, the most common pathogens identified in a cohort of children at TCH with co-morbidities and central venous lines included: *Staphylococcus aureus, Pseudomonas, and Enterobacter*.

Inclusion Criteria: All pediatric patients greater than 28 days old with a temperature abnormality and/or concern for infection AND who meet one of the following criteria:

- Three or more of the identified signs and symptoms of shock (Table 3) and/or abnormal vital signs (Table 2)
- High risk patient (Table 1) AND two or more of the identified signs and symptoms of shock (Table 3) and/or abnormal vital signs (Table 2)
- Hypotension (refer to Table 2)

**Table 1. High Risk Conditions**

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignancy</td>
</tr>
<tr>
<td>Sickle Cell Disease and other patients with asplenia</td>
</tr>
<tr>
<td>Bone marrow transplant</td>
</tr>
<tr>
<td>Central or indwelling line/catheter</td>
</tr>
<tr>
<td>Solid organ transplant</td>
</tr>
<tr>
<td>Severe mental retardation/cerebral palsy</td>
</tr>
<tr>
<td>Immunodeficiency, immunocompromised or immunosuppression</td>
</tr>
<tr>
<td>Urogenital abnormalities (i.e. spina bifida)</td>
</tr>
</tbody>
</table>

**Table 2. PALS Adjusted Vital Signs for Septic Shock**

<table>
<thead>
<tr>
<th>Age</th>
<th>Heart Rate</th>
<th>Resp Rate</th>
<th>Systolic BP</th>
<th>Temp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0d - 1m</td>
<td>205</td>
<td>&gt; 60</td>
<td>&lt; 60</td>
<td>&lt;36 or &gt;38</td>
</tr>
<tr>
<td>&gt; 1m - 3m</td>
<td>205</td>
<td>&gt; 60</td>
<td>&lt; 70</td>
<td>&lt;36 or &gt;38</td>
</tr>
<tr>
<td>&gt; 3m - 1y</td>
<td>190</td>
<td>&gt; 60</td>
<td>≤ 70</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt; 1y - 2y</td>
<td>190</td>
<td>&gt; 40</td>
<td>&lt; 70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt; 2y - 4y</td>
<td>140</td>
<td>&gt; 40</td>
<td>&lt; 70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt; 4y - 6y</td>
<td>140</td>
<td>&gt; 34</td>
<td>&lt; 70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt; 6y - 10y</td>
<td>140</td>
<td>&gt; 30</td>
<td>&lt; 70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt; 10y - 13y</td>
<td>100</td>
<td>&gt; 30</td>
<td>&lt; 90</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt; 13y</td>
<td>100</td>
<td>&gt; 20</td>
<td>&lt; 90</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
</tbody>
</table>

**Table 3. Signs and Symptoms of Shock**

<table>
<thead>
<tr>
<th>Sign and/or Symptom</th>
<th>HR followed by BP changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased or weak capillary refill</td>
<td></td>
</tr>
<tr>
<td>Bounding</td>
<td></td>
</tr>
<tr>
<td>≥ 3 sec Capillary refill</td>
<td></td>
</tr>
<tr>
<td>Flash (&lt; 1 sec)</td>
<td></td>
</tr>
<tr>
<td>Mottled, cool</td>
<td></td>
</tr>
<tr>
<td>Petechiae below the nipple, any purpura</td>
<td></td>
</tr>
</tbody>
</table>
| Decreased, irritability, confusion inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtundation | *HR followed by *BP changes will be noted as shock becomes uncompensated.

**Exclusion Criteria:**

- Trauma
- Neonates (0-28 days old)
- Pregnancy
- Age > 18 years

**Differential Diagnosis:**

- Anaphylaxis
- Hypovolemia
- Urinary tract infection
- Fever without localizing symptoms
- Central line associated blood stream infection
- Congestive Heart Failure
- Neurogenic shock
- Sepsis
- Pneumonia
- Meningitis

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Septic Shock in Neonates (10,11)
The signs of septic shock in the neonate are non-specific including respiratory distress, poor perfusion, tachycardia, temperature instability, inadequate feeding, poor tone, pale color, and tachypnea. Differential diagnoses for the newborn with suspected septic shock includes disseminated bacterial, viral, or fungal infection, congenital heart disease (CHD), inborn errors of metabolism, and perinatal asphyxia. If the neonate has fever, CSF pleocytosis, and is ill appearing, congenital viral infection such as Herpes Simplex Virus (HSV) should be considered in the differential diagnosis and testing for HSV should be sent from blood and CSF. Risk factors such as maternal history of chorioamnionitis, prolonged rupture of membranes, or maternal HSV infection at the time of delivery should be taken into consideration in the evaluation process.

If the patient is admitted from home and presenting with signs of CHD related septic shock, initial evaluation should occur in the CVICU. An echocardiogram can be a vital diagnostic tool in delineating the underlying cause of septic shock in infants presenting with signs of shock. Vascular access should be established and dextrose containing maintenance IV fluids should be given while evaluation is in progress. An umbilical venous catheter is the preferred vascular access in neonates with suspected septic shock within the first week of life if the umbilical vein is patent and viable. If the patient is hypovolemic, treatment should be initiated with crystalloid fluid boluses of 10 ml/kg. Low dose dopamine (5 mcg/kg/min) or epinephrine should be started and titrated as necessary to optimize perfusion. Packed red blood cells can be administered for treatment of anemia. If the patient is presenting from home, empiric antibiotic treatment can be initiated with antibiotics tailored based on age at presentation (early onset sepsis versus late onset sepsis). Previously hospitalized neonates with suspected septic shock should be empirically treated with antibiotics as specified in Baylor College of Medicine (BCM) guidelines. If suspecting meningitis, using a third generation cephalosporin can be considered for providing adequate CSF penetration. If suspected HSV infection, consider empiric treatment with acyclovir, especially in the setting of pneumonitis, hepatitis, coagulopathy, hypoglycemia, or vesicles.

Diagnostic Evaluation: A brief history and physical examination should be conducted concurrently with the prompt initiation of treatment.

History: Assess for
• Temperature instability
• Poor feeding
• Changes in mental status
• Difficulty breathing
• Decreased urine output
• Comorbid conditions

Physical Examination: (1,9,10)
The severity of the inflammatory response associated with septic shock increases over a continuum. Early signs and symptoms of septic shock are a result of the body’s compensatory mechanisms while late signs are indicative of decompensation. Assess for the early indications of shock along with the signs below:
• Widened pulse pressure due to decreased diastolic pressures
• Normal systolic blood pressure

As the body begins to decompensate and organ dysfunction progresses, the late signs of shock be assessed. The patient may also exhibit: (1,9)
• Rapid shallow breathing
• Decreased respiratory rate
• Oliguria
• Cyanosis
• Hypotension

Continuously monitor:
• Heart rate and rhythm
• Oxygen saturation
• Blood pressure

Frequently Monitor:
• Temperature
• Urine output

Laboratory Tests: There is no single laboratory test that reliably predicts or confirms a patient’s initial condition. Blood cultures are an essential part of the evaluation of septic shock. A trend in procalcitonin or lactate levels may be helpful when incorporated with clinical judgment.

<table>
<thead>
<tr>
<th>Lab Test</th>
<th>Required</th>
<th>Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood culture</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Complete blood count (CBC) with platelet and differential</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Blood gas with Metabolites</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Chem 10 panel</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lactate</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
**Evidence Supports**

- Abnormal vital signs and indications of poor perfusion are the signs and/or symptoms that most reliably predict or confirm septic shock. *(8,12-15)* - Strong recommendation with low quality evidence

- Implement methods for early recognition of shock by non-physicians in order to improve outcomes. *(8,16-18)* - Strong recommendation with low quality evidence

- Initiate treatment consistent with PALS guideline prior to ED arrival for patients with suspected septic shock. *(14)* - Strong recommendation with low quality evidence

- Three boluses of 20 mL/kg of crystalloid fluid should be administered intravenously via push-pull, rapid infuser, or pressure bag with the first bolus given within 20 minutes of recognition of septic shock. *Adjust fluid volume and rapidity of administration for patients whose pre-existing condition precludes rapid, large volume fluid resuscitation.* *(14,19-29)* - Strong recommendation with moderate quality evidence

Remarks – There is an ongoing prospective randomized trial in progress comparing the effectiveness of lactated Ringer’s versus normal saline for initial resuscitation in children with suspected sepsis. The content expert team will await results from this trial to determine if revisions should be made to this recommendation.

- Epinephrine (0.05 mcg/kg/min) or norepinephrine (starting dose: 0.05 mcg/kg/min) should be started in patients with fluid refractory shock. Vasopressor treatment should be tailored based on the patient’s hemodynamic state. *(30-37)* – Strong recommendation with low quality evidence

Remarks
  - Evidence supports starting with at least the minimum dose listed above. These medications may be titrated up to achieve the desired effect up to a maximum of:
    - Epinephrine MAX 1 mcg/kg/min
    - Norepinephrine MAX 2 mcg/kg/min

- Patients with malignancies, asplenics, a history of bone marrow transplant, central or indwelling lines/catheters, history of solid organ transplant, severe mental retardation and/or cerebral palsy, immunodeficiency, immunocompromise, or immunosuppression, and/or urogenital abnormalities have an increased risk of septic shock. *(4,8,14,25-26,38)* - Strong recommendation with low quality evidence

- Administer vancomycin and ceftriaxone as empiric antibiotics to previously healthy patients with suspected septic shock (including children with sickle cell disease or suspicion of meningitis). Nafcillin should be added for suspected Staphylococcus infections. *(3,6,13,39-40)* - Strong recommendation with moderate quality evidence

- Administer vancomycin and cefepime as empiric antibiotic treatment for immunocompromised and other high risk patients with suspected septic shock (excluding children with asplenia or sickle cell disease). Gentamicin should be added to the empiric treatment regimen for the subset of patients within this group that are unstable. In patients with a recent history (past 3 to 6 months) of multidrug-resistant organisms, consult the Infectious Disease service and consider adding a carbapenem empirically. *(6,41-44)* - Strong recommendation with moderate quality evidence

- Consider administration of stress-dose steroids for patients with catecholamine resistant shock. Consider obtaining a random cortisol level prior to administration of steroids, when feasible. *(45-49)* - Weak recommendation with very low quality evidence

- Consider treatment for anemia in patients with suspected septic shock. *(50)* – Weak recommendation with very low quality evidence

**Evidence Lacking/Inconclusive**

- Alternative methods for fluid delivery should be pursued, including intraosseous access, if rapid intravenous access is not obtained in a timely fashion in order to provide the first fluid bolus within 20 minutes of the recognition of septic shock. – Consensus recommendation

- Oxygen should be titrated to keep oxygen saturations within the patient’s normal range. – Consensus recommendation

**Evidence Against**

- Single laboratory tests should not be used to inform about a patient’s initial condition. *(51-62)* – Strong recommendation with low quality evidence

- Prediction models should not be applied during the initial management of patients with septic shock to identify patients at risk for multiple organ failure. *(63-65)* – Strong recommendation with low quality evidence
Condition-Specific Elements of Clinical Management

**Treatment Recommendations:**

**Phase 1 – Within five (5) minutes** from recognition of septic shock initiate the following:
- Cardiac monitors and continuous pulse oximetry
- Vital signs every 15 minutes
- Neuro vital signs every 30 minutes
- Administer supplemental oxygen therapy and/or respiratory support to keep oxygen saturations within patient’s normal range.
- Strict intake and output

**Phase 2 – Within twenty (20) minutes** from recognition of septic shock initiate the following:
- Establish peripheral IV. If IV unattainable, start IO access.
- Draw labs on IV placement
- Completion of first fluid bolus of 20 mL/kg of crystalloid fluid intravenously (Table 4)
- Reassess for need of additional fluid resuscitation
- Consider inserting a foley catheter

**Phase 3 – Within sixty (60) minutes** from recognition of septic shock initiate the following:
- Administer antibiotics (Table 5)
- Establish second PIV (or IO if PIV cannot be established) and consider central line if not done.
- Consider 2nd and 3rd bolus of 20 mL/kg NS or colloid fluid up to and over 60 mL/kg until perfusion improves or unless rales or hepatomegaly develops (Table 4)
- Correct hypoglycemia and/or hypocalcemia, if necessary
- Consider treatment for anemia
- If patient on chronic steroids, give stress dose for adrenal insufficiency.
- Reassess for need of additional fluid resuscitation

**Phase 4 – Fluid Refractory Shock**
- Transfer to the ICU
- Evaluate hemodynamic state
- Reverse fluid refractory shock by titrating epinephrine (dose range: 0.05 to a MAX of 1 mcg/kg/min) or norepinephrine (dose range: 0.05 to a MAX of 2 mcg/kg/min).
- Obtain central access if it does not delay admission to ICU. Initiate venous saturation and central venous pressure monitoring.
- Reassess for need of additional fluid resuscitation

**Phase 5 – Catecholamine Resistant Shock**
- Administer hydrocortisone at a dose of 2 mg/kg (Table 7)
- When feasible, send a random cortisol level prior to steroid administration to help guide treatment once stabilized.
- If patient is resistant to fluids and catecholamines, then look for other causes of shock including:
  - Pericardial effusion
  - Tension pneumothorax
  - Abdominal compartment syndrome
  - Ongoing blood loss
  - Necrotic tissue
  - Inadequate source control infection
- Consider ECMO if prior interventions are not effective

**Therapeutic End Points**

Treatment for septic shock should be aimed at achieving the end points below:
- Normal mental status
- Age-appropriate vital signs (HR, RR, blood pressure)
- Capillary refill <3 secs
- Palpable distal pulses without a differential from central pulses
- Urine output >1 mL/kg/hr
- Warm extremities
- Normal glucose and ionized calcium concentration
- Mixed venous oxygen saturation >70%

**Measures:**

**Outcomes**-
- Mortality rate

**Process**-
- Number of times best practice alert (BPA) triggered and not shock patient
- Utilization of the shock order sets all phases
- Utilization of other order sets as defined in BPA
- Percentage of patients administered fluids within 20 min of recognition of shock
- Time to antibiotic administration after recognitions of shock
- Number of patients admitted and shock recognized after admission to inpatient unit within 12 hours
- Appropriate antibiotics administered (high risk vs. low risk)
**Table 4. Bolus**

<table>
<thead>
<tr>
<th>Bolus 1 - Within 20 min of identification of shock then reassess need for additional fluids up to 3 boluses</th>
<th>Route: IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium CHLORide 0.9% (NS)</td>
<td>20 mL/kg Push/pull or rapid infuser</td>
</tr>
<tr>
<td>Patients whose condition prohibits rapid fluid resuscitation</td>
<td>Route: IV</td>
</tr>
<tr>
<td>Sodium CHLORide 0.9% (NS)</td>
<td>10 mL/kg Push/pull or rapid infuser</td>
</tr>
</tbody>
</table>

**Table 5. Antibiotics**

<table>
<thead>
<tr>
<th>Antibiotic Therapy</th>
<th>Previously Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>Route: IV 50 mg/kg MAX: 2000 mg/dose</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Route: IV 15 mg/kg MAX: 1500 mg/dose</td>
</tr>
<tr>
<td>Add for suspected Staph Infection</td>
<td>Route: IV 50 mg/kg MAX: 2000 mg/dose</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>Route: IV 100 mg/kg MAX: 3000 mg/dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotic Therapy</th>
<th>Sick Cell Disease or other asplenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>Route: IV 50 mg/kg MAX: 2000 mg/dose</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Route: IV 15 mg/kg MAX: 1500 mg/dose</td>
</tr>
<tr>
<td>Add for suspected Staph Infection</td>
<td>Route: IV 50 mg/kg MAX: 2000 mg/dose</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>Route: IV 100 mg/kg MAX: 3000 mg/dose</td>
</tr>
<tr>
<td>Add for suspected intra-abdominal infection</td>
<td>Route: IV 100 mg/kg MAX: 3000 mg/dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotic Therapy</th>
<th>Immunocompromised and/or High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefepime</td>
<td>Route: IV 50 mg/kg MAX: 2000 mg</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Route: IV 15 mg/kg MAX: 1500 mg/dose</td>
</tr>
<tr>
<td>Unstable patients</td>
<td>Route: IV 2.5 mg/kg MAX: 120 mg/dose</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Route: IV 7.5 mg/kg MAX: 500 mg</td>
</tr>
<tr>
<td>Suspected intra-abdominal process</td>
<td>Route: IV 2.5 mg/kg MAX: 120 mg/dose</td>
</tr>
</tbody>
</table>

**Table 6. Pressors**

| Tailor vasopressor treatment based on hemodynamic state: |
|---|---|
| EPINEPHrine | Route: Continuous IV infusion 0.05 mcg/kg/min Titrate to a MAX of 1 mcg/kg/min |
| Norepinephrine | Route: Continuous IV infusion 0.05 mcg/kg/min Titrate to a MAX of 2 mcg/kg/min |

**Table 7. Steroids**

| Catecholamine Resistant Shock |
|---|---|
| Hydrocortisone sodium succinate | Route: IV 2 mg/kg MAX dose: 200 mg |
Recognize abnormal vital signs and altered mental status and perfusion

Within 5 min of arrival or recognition:
- Administer supplemental oxygen and/or respiratory support to keep oxygen saturation in normal range
- Insert PIV. If IV unattainable, establish IO access.
- Place on cardiac monitor and continuous pulse oximeter
- Vital signs every 15 min.
- Neuro checks every 30 min.
- Strict I & O’s

Initial Resuscitation
Within 20 min. of arrival or recognition:
- Administer 1st bolus of 20 mL/kg normal saline (NS) via push-pull, rapid infuser or pressure bag within 20 minutes
- Reassess need for additional fluid resuscitation
- Draw labs
- Begin antibiotics within 60 minutes
- Consider inserting a foley catheter

ICU Transfer Criteria
- Vital signs and/ or neurological signs every hour or more frequent as ordered
- Intubation and/or acute ventilatory assistance
- Vasoactive drugs to maintain cardiovascular status
- Clinical concern for deterioration
- Arterial Cannulation

Hypoglycemia Treatment
ID10W 5 ml/kg/dose IV/IO
ID25 2 ml/kg/dose IV/IO
ID25 should be administered for children > 1 year old.

Subsequent Resuscitation
- Establish second PIV (or IO if PIV cannot be established) and consider central line.
- Administer 2nd and 3rd boluses of 20 mL/kg isotonic saline or colloid up to and over 60 mL/kg until perfusion improves or unless rates or hematomegaly develop
- Correct hypoglycemia and/or hypocalcemia
- Consider treatment of anemia
- If on chronic steroids, give stress dose.
- Reassess need for additional fluid resuscitation

Fluid Refractory Shock
- Transfer to ICU
- Tailor vasoressor treatment based upon the patient’s hemodynamic state. Epinephrine or norepinephrine can be started at the doses below.
  - Titrate epinephrine (dose range: EPINEPHrine 0.05 to 1 mcg/kg/min) via IV or central access.
  - Titrate central norepinephrine (dose range: 0.05 to 2 mcg/kg/min) via central access
- Obtain central access if it does not delay admission to the ICU. Initiate venous saturation and central venous pressure monitoring

Catecholamine Resistant Shock
- Begin hydrocortisone if at risk for absolute adrenal insufficiency (Dosage: 2 mg/kg IV bolus). Obtain serum cortisol level prior to administration, if feasible.
- Consider ECMO if prior interventions are not effective

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References


44. Texas Children’s Hospital Susceptibility Data. (2014). Antibiotic susceptibility in gram negative organisms for 53 individual patient isolates in the hematology/oncology population. Available from the TCH Pathology Database.


Clinical Standards Preparation
This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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Development Process
This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts

2. Review of Existing Internal and External Guidelines

3. Literature Review of Relevant Evidence
   - Searched: Medline, Cochrane, AHRQ, Cinahl, AAP, Google Scholar, American College of Critical Care Medicine, American Heart Association, Guideline Clearing House

4. Critically Analyze the Evidence
   - Three systematic reviews, eleven meta-analyses, six randomized controlled trials, thirty-six non-randomized studies, four professional organization guidelines

5. Summarize the Evidence

- Materials used in the development of the guideline, evidence summary, and order sets are maintained in a Septic Shock evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence
Published clinical guidelines were evaluated for this review using the AGREE II criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence in support of or against specific interventions and identifies where evidence is lacking/inconclusive. The following categories describe how research findings provide support for treatment interventions.

- “Evidence Supports” provides clear evidence that the benefits of the intervention exceed harm.
- “Evidence Against” provides clear evidence that the intervention is likely to be ineffective or that it is harmful.
- “Evidence Lacking/Inconclusive” indicates there is currently insufficient data or inadequate data to support or refute a specific intervention.

The GRADE criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Quality</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>Desirable effects clearly outweigh undesirable effects or vice versa</td>
<td></td>
</tr>
<tr>
<td>Weak</td>
<td>Desirable effects closely balanced with undesirable effects</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence</td>
<td></td>
</tr>
<tr>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from un systemctlic clinical observations or very indirect evidence</td>
<td></td>
</tr>
</tbody>
</table>

Recommendations
Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the recognition and initial management in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process
Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved with every review and update.

Disclaimer
Practice recommendations are based upon the evidence available at the time the guideline was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care, and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent
judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient family, to make the ultimate judgment regarding care.

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<tr>
<th>Date</th>
<th>Action</th>
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<tr>
<td>May 2015</td>
<td>First Iteration</td>
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<tr>
<td>Jan 2017</td>
<td>Revision and Update</td>
<td>Vasopressor evidence update</td>
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<td>Change to antibiotic dosing</td>
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<td>Jan 2019</td>
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